May 10, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9847-Final.doc).

Title: Autoimmune Pancreatitis in the Context of IgG4-Related Disease: Review of Imaging Findings

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript No.: 9847

The manuscript has been improved according to the suggestions of reviewers:

1. Manuscript format has been updated.
2. Responses to Reviewer 1.
    a. "There were few image data to support this. It is necessary to present representative image data, because this review article dealt with important role of imaging in AIP. Could you show representative images of various modalities?
        i. Response: Thank you for this thoughtful response. We have added a number of CT, MR, and ERCP images, focusing on AIP findings, described below. We thank you for this insightful opportunity to augment and enrich the manuscript with representative images.
    b. Could you show how delayed enhancement by CT or MRI differentiate between AIP and pancreatic cancer? Could you show imaging to support this?"

i. Response: A new figure, presently labeled Figure 2, has been added, demonstrating enhancement abnormalities on CT and MR imaging in a patient with focal AIP in the pancreatic tail. Specifically, arterial hypo-enhancement (CT, MR), with delayed enhancement (MR), is depicted, along with a follow-up image demonstrated resolution of enhancement abnormality after treatment (CT).

c. "Could you show typical ERCP findings of AIP including diffuse irregular narrowing of MPD and bile duct strictures? Could you show useful ERCP image findings in the differentiation between AIP and pancreatic cancer?"

i. Response: A new figure, presently labeled Figure 3, has been added, demonstrating ERCP findings of diffuse MPD and segmental narrowing of the CBD. A CT image of intrahepatic biliary ductal dilatation is also included.

d. "Could you show representative EUS findings of AIP?"

i. Response: We thank the reviewer for this suggestion. However, we could not obtain EUS images of AIP. We refer readers to References 15 and 33, as described in Section 3.2.

e. "Could you show useful FDG-PET image findings in the differentiation between AIP and pancreatic cancer?"

i. Response: FDG-PET is highly sensitive in both AIP and pancreatic cancer. Extra-pancreatic findings demonstrated by FDG-PET may represent extra-pancreatic manifestations of IgG4-related disease, or metastatic lesions in pancreatic cancer. This discussion is expanded and added to section 4.3.

To reflect these changes, ‘Extra-pancreatic lesions’ has been removed from Table 1.

f. “Could you show typical image of IgG4 related renal disease?”
    i. Response: We thank the reviewer for this suggestion. However, we could not obtain images of IgG4-related renal disease. We refer readers to references 69 and 70, as described in Section 6.1.

g. “Could you show representative extra-pancreatic lesions other than head and neck findings, such as lung lesions and bile duct lesions?”
    i. Response: Examples of extra-pancreatic FDG-avid lesions are provided in the presently labeled Figure 5.

3. Responses to Reviewer 2.

a. “In 2.2 Diagnostic features of IgG4-related disease (page 7), the authors stated that additional clinical, laboratory, and histopathological findings increase the sensitivity. Japanese consensus criteria, which aim to rule out malignancy, has less sensitivity but high specificity. Therfore, the authors should emphasize this point. Improvement of sensitivity is obtained at the cost of specificity.”
    i. Response: Section 2.2 has been revised to reflect this important point.

b. “In 2.2 Diagnostic features of IgG4-related disease (page 7), the authors stated that up to 30% of patients with IgG4-related disease may have normal serum IgG4 levels, but the IgG4 positive ratio might differ between type 1 and type 2 diseases.”
    i. Response: The relevant sentence in Section 2.2 has been clarified to reflect this important point.

c. “In 3.2. Endoscopic techniques (page 9), the authors should discuss the role of IDUS at the time of ERCP as an adjunct to evaluate biliary stricture (Gastrointest Endosc. 2010;71:85-90.).”

    i. Response: This is an important topic and has been added to the discussion in Section 4.2

d. “As the authors repeatedly discussed, differentiation of AIP from pancreatic cancer is an important issue. The accuracy of EUS-FNA is well established and EUS-FNA is routinely used to get a pathological diagnosis of pancreatic lesions. The utility of EUS-FNA using a 19-gauge needle was also reported (Clin Gastroenterol Hepatol. 2012;10:316-22.). Please discuss the role of EUS-FNA in AIP and IgG4 related diseases.”

    i. Response: This is an important topic and has been added to the discussion in Section 4.2. The role of EUS-FNA in AIP and IgG4-related disease is an important one, and a reference to a recent review on the topic has been added to the discussion in Section 4.2 (PMID: 24712522).

e. “In 3.3 Magnetic resonance cholangiopancreatography (page 10), Kamisawa et al. reported that MRCP cannot diagnose AIP because the narrowed segments are not visualized but it may have role after treatment (Abdom Imaging. 2009;34:381-4.). Please discuss.”

    i. Response: This is an important point and has been clarified in the discussion in 3.3.

f. “In 3.5. PET imaging (page 12), the authors specifically discussed PET findings, but gallium-scintigram is reported to be useful in assessing extra-pancreatic lesions. Please discuss.”

i. Response: This is an important point and has been added to Section 6.

4. References and typesetting were corrected. DOI requirement was fulfilled.
5. Formatting of Figures and Legends was corrected.

a. Decomposable Figures are provided in a separate file (Figures_Revised.ppt).

Thank you again for your consideration of our manuscript for publication in the *World Journal of Gastroenterology.*

Sincerely yours,

Dushyant Sahani, MD and Leslie Lee, MD

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